II. REMARKS

Preliminary Remarks

Reconsideration and allowance of the present application based on the following remarks are respectfully requested. Claims 8, 10-16, 18, and 19 have been canceled because these claims were withdrawn from further consideration as being drawn to a non-elected invention, and not for any reason related to patentability. Claims 1-7, 9, and 17 were cancelled and rewritten as claims 20-36 as a convenience to the examiner.

The applicants have amended the specification at page 18, lines 1-5 to indicate the address of the biological depository where plasmid Top10/pCR2.1menEint was previously deposited. No new matter is believed to have been introduced herein.

New claim 20 is directed to an isolated nucleic acid comprising a nucleotide sequence selected from the group consisting of (a) the nucleotide sequence as set forth in SEQ ID NO: 1; (b) a nucleotide sequence encoding the polypeptide as set forth in SEQ ID NO:2; (c) a nucleotide sequence fully complementary to (a) or (b). Support for new claim 20 can be found throughout the specification, for example, on page 2, lines 29 and 30 and page 4, lines 17-21, original claim 7, and page 3, line 8.

New claim 21 is directed to an isolated nucleic acid comprising a nucleic acid sequence that is at least 90% identical to the sequence of the nucleic acid sequence of claim 20 and encodes a polypeptide that has O-succinylbenzoic acid CoA ligase activity. Support for the phrase "at least 90% identical to the sequence" and O-succinylbenzoic acid CoA ligase activity can be found throughout the specification, for example, from page 3, lines 4 and 5, page 6, lines 21-23, and page 4, line 31 to page 5, line 3.

New claim 22 is directed to an isolated nucleic acid comprising a nucleic acid sequence that is at least 95% identical to the sequence of the nucleic acid sequence of claim 20 and encodes a polypeptide that has O-succinylbenzoic acid CoA ligase activity. Support for the phrase "at least 95% identical to the sequence" can be found throughout the specification, for example, from page 4, line 31 to page 5, line 3.

New claim 23 is directed to an isolated nucleic acid that encodes a polypeptide that has O-succinylbenzoic acid CoA ligase activity and hybridizes to the complement of the nucleic acid of claim 20 under the following stringent conditions: a final wash in 0.1X SSC at 68°C. Support for the phrase "a final wash in 0.1X SSC at 68°C" can be found throughout the specification, for example, on page 9, lines 18-34.

New claim 30 is directed to an isolated nucleic acid consisting of SEQ ID NO: 1 or a fragment thereof and encoding a polypeptide that has O-succinylbenzoic acid CoA ligase activity. Support for the phrase "fragment thereof" can be found throughout the specification, for example, on page 15, lines 1-3, and Examples 3 and 4.

New claim 31 is directed to an isolated nucleic acid consisting of a fragment of at least 40 consecutive nucleotides of SEQ ID NO: 1 or the full complement thereof. New claim 32 is directed to the isolated nucleic acid of claim 31, wherein said fragment is a primer or probe. Support for the phrase "fragment of at least 40 consecutive nucleotides of SEQ ID NO: 1 or the full complement thereof" and "primer or probe" can be found throughout the specification, for example, on page 4, lines 10-16 and 17-26.

New claims 24-29 are directed to the nucleic acids of claims 20-23 in vectors, host cells wherein the vector is an integration vector pCR.1menEint having an internal fragment of the *men*E gene 520 bp in size; and a restriction map as set forth in Fig. 1 and wherein the vector has been deposited in the *E. coli* strain Top10/pCR.2menEint under accession no. DSM 14080. Similarly, new claims 33-36 are directed to the nucleic acids of claims 30-32 in vectors and host cells. Support for these new claims can be found throughout the specification, for example, original claims 9, and on page 18, lines 1-15 and Example 1.

The applicants do not intend by these or any amendments to abandon subject matter of the claims as originally filed or later presented, and reserve the right to pursue such subject matter in continuing applications.

Patentability Remarks

Rejection Pursuant to 35 U.S.C. §112, First Paragraph, Written Description

The examiner rejected claims 1-7 and 17 under 35 U.S.C. §112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the examiner alleged the claimed invention 70% claimed variants is not supported by a disclosure of any particular structure to function/activity relationship in the single disclosed species. In addition, the examiner alleged the specification fails to describe additional representative species of these polynucleotides by failing to identify structural characteristics or properties to predict the structure. The examiner, however, acknowledged the specification provides an

isolated polynucleotide consisting of SEQ ID NO: 1. The examiner concluded that the applicants have allegedly failed to sufficiently describe the claimed invention in full, clear, concise and exact terms for a skilled artisan to recognize applicants' were in possession of the claimed invention.

Solely for the purpose of expediting prosecution, and without prejudice to the applicants' right to seen broader claims in a continuing application, the applicants have canceled claims 1-7 and 17 without prejudice, thereby obviating the rejection of these claims. As discussed above, new claim 20 is directed to (a) nucleic acids comprising the nucleotide sequence of SEQ ID NO: 1, (b) nucleic acids that encode the amino acid sequence of SEQ ID NO: 2 and (c) nucleic acids that are fully complementary to (a) or (b). The examiner acknowledges that sequences (a) and (b) are fully described in the specification. [See Office Action, pages 4 and 5]. The applicants respectfully submit that nucleic acid sequences complementary to (a) or (b) are described from page 9, line 18 to page 20, line 2 and page 3, lines 6-17.

New independent claims 21-23 and 30-32 are directed to nucleic acid that are at least 90% or 95% identical to SEQ ID NO: 1, and that exhibit O-succinylbenzoic acid CoA ligase activity and fragments of nucleic acids that encode a polypeptide having O-succinylbenzoic acid CoA ligase activity. These structural and functional characteristics of the subject matter of new claims 21-23 and 30-32 meet the Written Description Guidelines of the United States Patent Office (February, 2000). In particular, Example 14 of the guidelines states that a claimed variant polynucleotide that has a high percent identity to a sequence taught in the specification, along with a functional limitation that the claimed variant polynucleotides encode variant polypeptides that exhibit a specified catalytic activity, meet the written description if the required activity can be determined as described in the specification. In the instance claims, the claimed variants must each be at least 90% or 95% identical to SEQ ID NO: 1(page 4, line 31 to page 5, line 3) and encode a polypeptide that retains the specified O-succinylbenzoic acid CoA ligase activity. These biological activities may be measured in assays well known in the art. In addition, the specification teaches that coryneform bacteria produce amino acids like lysine, in an improved manner after attenuation of the menE gene. Example 5 demonstrates that the menE knockout *C. glutamicum* strain DSM5715::pCR2menEint increased its lysine production (see Table 1) when using a PCR generated fragment 520 bp of the SEQ ID NO:1. In addition, the polynucleotides of claim 20 that hybridize under the high stringent hybridization conditions set forth in claim 23 are

explicitly supported in the specification at page 9, lines 18-34. The nucleic acids of claim 30 are described in page 5, lines 1-3 and measuring for O-succinylbenzoic acid CoA ligase activity is well known in the art. The nucleic acids of at least 40 consecutive nucleotides of SEQ ID NO: 1, which can serve as primers or probes are described on page 4, lines 10-16 and 17-25.

Accordingly, the structural and functional limitations of claims 20-23 and 30-32 are described in the specification in such a way as to convey to one of skill in the art that the applicants had possession of a finite number of claimed polynucleotides.

Claims 24-29 and 33-36 ultimately depend from claims 20-23 and 30-32 (*e.g.*, vectors comprising such a polynucleotide, host cells comprising such vectors, and deposit strains) and therefore are fully described in the specification.

In view of the foregoing amendments and remarks, the applicants submit that the rejection of claims 1-7 and 17 pursuant to 35 U.S.C. § 112, first paragraph, for lack of written description, is moot, and a rejection of new claims 20-36 on the same grounds would be improper.

Rejection Pursuant to 35 U.S.C. §112, First Paragraph, Enablement

In paragraph 5 of the official action, the examiner rejected claims 1-3, 5-7, and 17 under 35 U.S.C. §112, first paragraph, for lacking enablement. Specifically, the examiner stated that while the isolated polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 or an isolated polynucleotide comprising SEQ ID NO: 1 is enabled by the specification, any polynucleotide that is at least 70% identical to the polynucleotide encoding a polypeptide that contains the amino acid sequence of SEQ ID NO: 2, a polynucleotide that encodes a polypeptide that is at least 70% identical to the amino acid sequence of SEQ ID NO: 2, and a polynucleotide containing at least 15 successive nucleotides thereof is not enabling.

Solely for the purpose of expediting prosecution, and without prejudice to the applicants' right to seek broader claims in a continuing application, the applicants have canceled claims 1-3, 5-7, and 17 thereby rendering moot the rejection as applied to each of these claims. New claim 20 is directed to (a) nucleic acids comprising the nucleotide acid sequence of SEQ ID NO: 1, (b) nucleic acids that encoding the polypeptide as set forth in SEQ ID NO: 2 and (c) polynucleotides that are complementary to (a) or (b). The examiner acknowledges that the sequences of part (a) and (b) are enabled by the specification. [See

office action, paragraph 5, page 4.] Polynucleotides that are complementary are also taught by the specification on page 3, lines 5-16 and are readily identifiable by one of skill in the art. Claims ultimately dependent on claim 20, further limit the enabled polynucleotides to, e.g., vectors comprising such a polynucleotide, host cells comprising such vectors, deposit host strains comprising such vectors, and the like. The instant application enables one of skill in the art to make and use the enabled nucleic acids in such well known applications. Accordingly, claim 20 and claims 24-29 which ultimately depend from claim 20, are enabled.

The applicant also submits that new claims 21-36 should not be rejected pursuant to 35 U.S.C. § 112, first paragraph, for lack of enablement. Claims 22 and 23 are directed to nucleic acids that comprise a nucleic acid sequence that is at least 90% or 95% identical to the nucleic acids of claim 20 and encode a polypeptide that has O-succinylbenzoic acid CoA ligase activity. The specification in Example 1 teaches how to identify polynucleotides that are at least 90% or 95% (see page 4, line 31 to page 5, line 3) identical to the nucleic acids of claim 41 that encode for the O-succinylbenzoic acid CoA ligase (see page 6, lines 22-24), that can integrate into the *C. glutaminum* chromosome at the menE gene chromosomal site (Example 4), and thus attentuate the menE gene of C. glutaminum which increases lysine production from this industrially important strain (as taught in Example 5).

New claim 23 is directed to nucleic acids that comprise a nucleic acid sequence that hybridizes to the complement of nucleotide sequences of claim 20 under stringent conditions. The specification teaches one of skill in the art how to identify these variant polynucleotide sequences. Page 23 of Example 4 provides a method to identify an integrated *men*E gene of SEQ ID NO: 1 in chromosomal DNA of *C. glutaminum* using stringent hybridization conditions (68°C at 0.1X SSC) as recited in claim 23. These methods provide guidance for identifying polynucleotides that hybridize under stringent conditions to the nucleic acid sequences of SEQ ID NO: 1. Further, the specification defines these highly stringent hybridization conditions (page 9, line 18 to page 10, line 2, provides methods for carrying out the hybridization reactions (Example 4), and provides several references for one of skill in the art to refer to, *e.g.*, DIG System Users Guide for Filter Hybridization of Boehringer Mannheim GmbH (Mannheim, Germany, 1993) and DIG Easy Hyb from Roche Diagnostics (page 23, lines 12-25; and page 10, lines 1-3).

New claim 30 is directed to an isolated nucleic acid that consists of SEQ ID NO: 1 or a fragment thereof. New claim 31 is directed to an isolated nucleic acid consisting of a fragment of at least 40 consecutive nucleotides of SEQ ID NO: 1 or the full complement

thererof. Both types of nucleotide fragments of SEQ ID NO: 1 are taught by the specification thus enabling one of skill in the art how to generate these fragments. For example in Example 3 of the specification, the applicants teach generating two SEQ ID NO: 1 fragments menE-int1 (SEQ ID NO: 3) and menE-int2 (SEQ ID NO: 4) as primers to amplify a 520 bp fragment of the menE gene to be used in knockout studies as outlined in Examples 4 and 5. These methods of Example 3 provide guidance to one of skill in the art to generate other primers to generate PCR fragments of the disclosed menE gene (SEQ ID NO:1) and assay for the functional O-succinylbenzoic acid CoA ligase activity. Further, the specification and claims define at least 40 oligonucleotides which can serve as probes and primers on page 4, lines 22-26 and that the fragments would have to encode for an O-succinylbenzoic acid CoA ligase activity.

The nucleic acids of new claims 20-23 and 30 are also functionally defined in that they are limited to those that encode a polypeptide having O-succinylbenzoic acid CoA ligase activity. This activity is readily assayable by one of skill in the art and attenuation of the menE gene can be measured by lysine production as taught in Example 5. In view of the structural and functional information about the claimed polynucleotides that is provided in the instant application, along with the instruction regarding how to use those polynucleotides, the applicants submit that the newly added claims 20-23, 30, and 31 are supported by an enabling disclosure.

As discussed above, claims 24-29 and 33-36 ultimately depend from claims 20-23 and 30-32 (*e.g.*, vectors comprising such a polynucleotide, host cells comprising such vectors, and deposit strains) and therefore are fully enabled by the specification.

In view of the foregoing amendments and remarks, the applicants submit that the rejection of claims 1-3, 5, 7, and 17 pursuant to 35 U.S.C. § 112, first paragraph, for lack of enablement, is moot and should be withdrawn, and a rejection of new claims 20-36 on the same grounds would be improper.

Rejection Under 35 U.S.C. §112, First Paragraph, Enablement

In paragraph 6 of the official action, the examiner rejected claim 9 under 35 U.S.C.§112, first paragraph, as containing subject matter not described in the specification to enable one skilled in the art to make or use the invention. Specifically, the examiner states

the novel gene and vector has been deposited in the transformed E.coli strain DSM 14080 but there was no indication in the specification as to the public availability.

The applicants submit herewith a declaration by the undersigned stating the specific microorganism has been deposited under the Budapest Treaty and a receipt of such deposit accompanies the declaration. Accordingly, the applicants submit that the rejection of claim 9 has been overcome and withdrawn and should not be extended to the new claims.

Rejection Under 35 U.S.C. §112, Second Paragraph, Indefiniteness

The examiner rejected claims 1-7 and 17 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicants regard as the invention.

The applicants have cancelled claims 1-7 and 17 and thereby the indefiniteness rejection is hereby moot. New claims 21-23 and 30 clearly direct their encoded polypeptides having O-succinylbenzoic acid CoA ligase activity since the menE gene encodes for this enzyme and direct support in the specification can be found on page 3, lines 4 and 5 and page 6, lines 21-24. New claim 23 is also directed specific hybridization conditions (0.1X SSC at 68°C) and is supported in the specification at page 9, lines 22-29.

Rejection Under 35 U.S.C. §102(b), Anticipation

In paragraph 10 of the official action, the examiner rejected claim 1 under 35 U.S.C. §102(b0 as being anticipated by Du Accession Number AD000004, which discloses a polynucleotide that contains at least 15 successive nucleotides encoding SEQ ID NO: 2.

The applicants have cancelled claim 1 thereby obviating the rejection. New claim 31 is directed to an isolated nucleic acid consisting of a fragment of at least 40 consecutive nucleotides of SEQ ID NO: 1 which would not fall within the scope of DU Accession Number AD 000004. Accordingly, the applicants respectfully submit the rejection of claim 1 is moot and should be withdrawn and a rejection on the same grounds of new claim 31 would be improper.

In paragraph 11 of the official action, the examiner rejected claims 5 and 6 under 35 U.S.C. §102(b) as being anticipated by Smith Accession No U5187. Specifically, the examiner alleges Smith teaches a polynucleotide that is expected to hybridize to SEQ ID NO: 1 since no stringent hybridization conditions have been recited. The applicants have cancelled claims 5 and 6 without prejudice. New claim 23 would not be anticipated by Smith

since this claim is directed to the stringent hybridization conditions of 0.1X SSC at 68°C. Accordingly, the applicants respectfully submit the rejection of claims 5 and 6 under 35 U.S.C. §102(b) is moot and a rejection on the same grounds of new claim 23 would be improper.

CONCLUSION

In view of the foregoing, the claims are now believed to be in form for allowance, and such action is hereby solicited. If any point remains in issue which the Examiner feels may be best resolved through a personal or telephone interview, please contact the undersigned at the telephone number listed below.

All objections and rejections having been addressed, it is respectfully submitted that the present application is in a condition for allowance and a Notice to that effect is earnestly solicited.

Respectfully submitted,

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